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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/701,453	04/16/2001	Dan M. Granoff	CHIR-0283	1041

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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1645	17

DATE MAILED: 12/03/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/701,453	GRANOFF ET AL.	
	Examiner	Art Unit	
	S. Devi, Ph.D.	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 September 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17-29* is/are pending in the application.

4a) Of the above claim(s) *29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *08 September 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

RESPONSE TO APPLICANTS' AMENDMENT

Applicants' Amendment

1) Acknowledgment is made of Applicants' amendment filed 09/08/03 (paper no. 16) in response to the non-final Office Action mailed 03/20/03 (paper no. 15).

Status of Claims

2) Claims 1-16 have been canceled via the amendment filed 09/08/03.

New claims 17-29 have been added via the amendment filed 09/08/03.

Claim 29 has been withdrawn from consideration since it is not drawn to the elected invention.

Claims 17-28 are pending and are under examination.

Prior Citation of Title 35 Sections

3) The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior Office Action.

Prior Citation of References

4) The references cited or used as prior art in support of one or more rejections in the instant Office Action and not included on an attached form PTO-892 or form PTO-1449 have been previously cited and made of record.

Objection(s) Withdrawn

5) The objection to the drawings made in paragraph 4 of the Office Action mailed 03/20/03 (paper no. 15) under 37 C.F.R 1.84 is withdrawn in light of Applicants' submission of formal drawings, which have been approved by the Draftsperson.

Objection(s) Maintained

6) The objection to the specification made in paragraph 6 of the Office Action mailed 03/20/03 (paper no. 15) with regard to the trademark recitations is maintained for reasons set forth therein.

Rejection(s) Moot

7) The rejection of claims 8-14 made in paragraph 11 of the Office Action mailed 03/20/03 (paper no. 15) under 35 U.S.C § 112, second paragraph, as being indefinite, is moot in light of Applicants' cancellation of the claims.

8) The rejection of claims 1-14 and 16 made in paragraph 12 of the Office Action mailed

03/20/03 (paper no. 15) under 35 U.S.C § 103(a) as being unpatentable over Granoff *et al.* (*Infect. Immun.* 65: 1710-1715, 01 May 1997 - Applicants' IDS) (Granoff *et al.*,1997) or Costantino *et al.* (*Vaccine* 10: 691-698,1992) and Milagres *et al.* (*FEMS Imunol. Med. Microbiol.* 13: 9-17, 1996 - Applicants' IDS) in view of Granoff *et al.* (*Vaccine* 11: S46-S51, 1993) (Granoff *et al.*, 1993) or Blake *et al.* (US 6,451,317, filed 09/08/1997), is moot in light of Applicants' cancellation of the claims. Applicants' arguments with regard to this rejection are considered moot.

New Rejection(s)

Applicants are asked to note the following new rejection(s) made in this Office. The new rejections are necessitated by Applicants' amendments, i.e., the submission of new claims.

Rejection(s) under 35 U.S.C § 112, First Paragraph (New Matter)

9) Claims 24 and 28 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Instant claims include the limitation: polylactic acids 'and/'or polyglycolic acids. Applicants point t page 4, lines 10-13 and page 3, lines 8-15 of the specification as providing descriptive support for these limitations. While there is support for a composition as claimed, comprising polylactic acid 'or' polyglycolic acid carrier, there appears to be no support for a composition comprising polyglycolic acids 'and' polylactic acids. Therefore, the limitation in the claims is considered to be new matter. *In re Rasmussen*, 650 F2d 1212 (CCPA, 1981). New matter includes not only the addition of wholly unsupported subject matter but also, adding specific percentages or compounds after a broader original disclosure, or even omission of a step from a method. See M.P.E.P 608.04 to 608.04(c).

Applicants are respectfully requested to remove the new matter from the claim(s), or invited to point to specific pages and line numbers in the originally filed specification where support for such a recitation can be found.

Rejection(s) under 35 U.S.C § 112, Second Paragraph

10) Claims 17-28 are rejected under 35 U.S.C § 112, second paragraph, as being indefinite, for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the

invention.

(a) Claim 17 is confusing in the recitation 'serogroup C **on** *N. meningitidis*'. To be consistent with the language used in the last line of the claim, it is suggested that Applicants replace the recitation with --serogroup C of *N. meningitidis*-- or --serogroup C *N. meningitidis*--.

(b) Analogous criticism applies to claim 26.

(c) In line 6 of claim 26, for clarity, it is suggested that Applicants replace the recitation 'of serogroup B of *N. meningitidis*' with --of serogroup B *N. meningitidis*--.

(d) Claim 19 has improper antecedence in the recitation 'said protein'. Claim 19 depends from claim 18 which recites 'a protein carrier', but not a 'protein'.

(e) Claim 22 is grammatically incorrect in the recitation 'are produced a deoxycholate extraction process'.

(f) In lines 2 and 3 of claim 20, in order to distinctly claim the subject matter, it is suggested that Applicants replace the recitation 'from serogroup C capsular polysaccharide' with --from *N. meningitidis* serogroup C capsular polysaccharide--.

(g) Claims 18-25, which depend directly or indirectly from claim 17, and claims 27 and 28, which depend directly or indirectly from claim 26, are also rejected as being indefinite, because of the indefiniteness or vagueness identified above in the base claim.

Rejection(s) under 35 U.S.C § 103

11) Claims 17-23 and 25 are rejected under 35 U.S.C § 103(a) as being unpatentable over Costantino *et al.* (*Vaccine* 10: 691-698,1992 - already of record) and van der Voort *et al.* (*Infect. Immun.* 64: 2745-2751, 1996) in view of Paradiso *et al.* (*Dev. Biol. Stand.* 87: 269-275, 1996).

Costantino *et al.* taught a conjugate vaccine comprising immunologically effective amounts of group C meningococcal oligosaccharides having a polymerization degree (DP) of up to 10 (i.e., about 12 repeating units) conjugated to CRM 197 and aluminium hydroxide adjuvant, and a method of inducing an immune response to group C *Neisseria meningitidis* by administering an immunologically effective amount of the vaccine to a subject (see page 693).

Costantino *et al.* do not teach the use of outer membrane vesicles from any strain, or from strain 44/76 of group B *Neisseria meningitidis* along with their conjugate vaccine.

However, van der Voort *et al.* disclosed an immunogenic group B meningococcal hexavalent

outer membrane vesicle vaccine from the group B meningococcal reference strain H44/76, which induced increased levels of bactericidal antibodies as well as a method of immunizing a mammal with the vaccine. The hexavalent vaccine advantageously covers more than 80% of the group B meningococcal subtypes isolated in many countries (see abstract; page 2745; Materials and Methods; Results; and Discussion).

Paradiso *et al.* taught that they have prepared immunogenic glycoconjugates of group C meningococcal saccharides covalently linked to the carrier CRM_{197} which elicited a booster response characteristic of a T-dependent response in humans. Paradiso *et al.* further taught that since group B meningococcal capsule is not very immunogenic in people, the alternative approach of using outer membrane vesicles from a virulent group B meningococcal strain has been sought (see page 272). Paradiso *et al.* expressly taught that outer membrane vesicles prepared from group B meningococcal strains contain an array of proteins and lipids, and that in future, it will be desirable to mix them with a vaccine comprising group C meningococcal conjugate to create a new set of formulation (see paragraph bridging pages 272 and 273).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine van der Voort's immunogenic group B meningococcal hexavalent outer membrane vesicle vaccine from the group B meningococcal reference strain H44/76 with Costantino's group C *Neisseria meningitidis* oligosaccharide-CRM_{197} conjugate vaccine to produce the instant invention, with a reasonable expectation of success, because Paradiso *et al.* expressly taught that it is desirable to mix a group C meningococcal conjugate with outer membrane vesicles prepared from group B meningococcal strains containing an array of proteins and lipids to create a new set of formulation. Since one of skill in the art would readily understand that Costantino's group C meningococcal oligosaccharide-containing vaccine would not induce immunity against group B meningococci, a major causative agent of meningitis, a skilled artisan would have been motivated to produce the instant invention for the expected benefit of not only eliciting antibodies against serogroup C meningococci, but also for eliciting advantageously bactericidal antibodies to, or for covering more than 80% of the group B meningococcal subtypes isolated in many countries as taught by van der Voort *et al.*

Claim 22 is a product-by-process claim which includes the process limitation: 'vesicles are

produced by a deoxycholate extraction process'. When claims are drawn to a product-by-process, claims are not limited to the manipulations of the recited step(s), but only the structure implied by the steps. MPEP § 2113 states:

> [E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process. *In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985)* (citations omitted).

A product does not have to be made by the same process in order to be the same product, because a product is a product, no matter how it is claimed. Applicants have not shown that the alleged difference(s) in the process results in a product that is structurally different from the product of the prior art. In the instant case, Applicants have not shown the underlying structure of the prior art group B meningococcal outer membrane vesicles differs from that of the instantly claimed vesicles.

Claims 17-23 and 25 are *prima facie* obvious over the prior art of record.

12) Claim 24 is rejected under 35 U.S.C § 103(a) as being unpatentable over Costantino *et al.* (*Vaccine* 10: 691-698,1992 - already of record) as modified by van der Voort *et al.* (*Infect. Immun.* 64: 2745-2751, 1996) and Paradiso *et al.* (*Dev. Biol. Stand.* 87: 269-275, 1996) as applied to claim 17 above, and further in view of Granoff (US 6,413,520, already of record) ('520).

The reference of Granoff ('520) is used in this rejection because it qualifies as prior art under 35 U.S.C § 102(e) and therefore is not disqualified as prior art under 35 U.S.C § 103(a).

The teachings of Costantino *et al.* as modified by van der Voort *et al.* and Paradiso *et al.* are explained above, which do not teach their composition to be further comprising polylactic acids and/or polyglycolic acids.

However, the use of polylactic acids and/or polyglycolic acids in combination with a meningococcal oligosaccharide conjugate was well known in the art at the time of the instant invention. For instance, Gronoff ('520) taught combining carriers, such as, polylactic and polyglycolic acids with meningococcal glycoconjugates for the purpose of primary vaccination wherein carriers do not themselves induce the production of harmful antibodies (see lines 1-10 in column 6).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to add Granoff's ('520) polylactic or polyglycolic acid to Costantino's

composition as modified by van der Voort *et al.* and Paradiso *et al.* to produce the instant invention, with a reasonable expectation of success. One of ordinary skill in the art would have been motivated to produce the instant invention for the expected benefit of providing Costantino's composition as modified by van der Voort *et al.* and Paradiso *et al.* for primary vaccination without inducing the production of harmful antibodies as taught by Gronoff ('520).

Claim 24 is *prima facie* obvious over the prior art of record.

Remarks

13) Claims 17-28 stand rejected.

14) Applicants' amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See M.P.E.P § 706.07(a). Applicants are reminded of the extension of time policy as set forth in 37 C.F.R 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

15) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center located in Crystal Mall 1. The transmission of such papers by facsimile must conform with the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The CM1 facsimile center's telephone number is (703) 308-4242, which is able to receive transmissions 24 hours a day and 7 days a week. The RightFax number for submission of before-final amendments is (703) 872-9306. The RightFax number for submission of after-final amendments is (703) 872-9307.

16) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (703) 308-9347. A telephone message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 7.15 a.m. to 4.15 p.m. except one day each bi-week which would be

disclosed on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909. The fax phone number for this Group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

November, 2003

S. DEVI, PH.D.
PRIMARY EXAMINER